The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte TERRY P. SNUTCH and DAVID L. BAILLIE

Appeal No. 2006-2389
Application No. 09/346,794

HEARD October 19, 2006

Before GRIMES, MILLS, and SCHEINER, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of identifying calcium channel antagonists, which the examiner has rejected for lack of utility. We have jurisdiction under 35 U.S.C. § 134. We reverse.

Background

"Calcium channels are a heterogeneous class of molecules that respond to depolarization by opening a calcium-selective pore through the plasma membrane. The entry of calcium into cells mediates a wide variety of cellular and physiological responses." Specification, page 1. Calcium channels "are also implicated in a number of human disorders." Page 2, first full paragraph.

"Native calcium channels have been classified by their electrophysiological and pharmacological properties as T, L, N, P and Q types. . . . T-type (or low voltage-activated) channels describe a broad class of molecules that activate at negative potentials and are highly sensitive to changes in resting potential." Page 2, last paragraph.

The specification discloses

> sequences for . . . mammalian calcium channel subunits of T-type calcium channels, . . . labeled as α_{1G}, α_{1H} and α_{1I} subunits. . . . [T]hese subunits, either alone or assembled with other proteins, can produce functional calcium channels, which can be evaluated in model cell lines to determine the properties of the channels containing the subunits of the invention. These cell lines can be used to evaluate[ ] the [e]ffects of pharmaceuticals and/or toxic substances on calcium channels incorporating α_{1G}, α_{1H} and α_{1I} subunits.

Page 7. "The complete cDNA sequences of the rat α_{1G}, α_{1H} and α_{1I} subunits are given by Sequence ID Nos. 23, 25 and 27, respectively." Page 16, first paragraph.

Discussion

1. Claims

Claims 28-31, 37, and 40 are pending and on appeal. Claim 28 is representative and reads as follows:

28. A method to identify an antagonist of a T-type calcium channel which method comprises:

a) contacting a recombinant cell expressing the α_1 subunit of a heterologous T-type calcium channel with a known agonist of said T-type calcium channel;

b) contacting said cell with a compound to be tested; and

c) determining the ability of said compound to diminish the activation of said α_1 subunit by said agonist;

wherein said α_1 subunit is functional as a T-type calcium ion channel and is encoded by a nucleotide sequence which hybridizes under conditions of stringency corresponding to washing at 62° C in 0.2 x SSPE/0.1% SDS to a nucleic acid comprising SEQ ID NO: 23 and

wherein said activating comprises enhancing the flow of calcium ions into said cell in the presence as compared to the absence of said agonist;

whereby a compound which diminishes the activation of said α_1 subunit by said agonist is identified as an antagonist.

Claim 28 is directed to a method of identifying compounds as T-type calcium channel antagonists, by contacting compounds with a recombinant cell expressing an α_1 subunit of a T-type calcium channel (encoded by a nucleic acid that hybridizes to SEQ ID NO:23 under specified conditions) and determining the ability of the compound to diminish the activation of the α_1 subunit by an agonist.

2. Utility

The examiner has rejected claims 28-31, 37, and 40 under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility. The examiner reasons that "[t]he T-type calcium channel of SEQ ID NO:23 has no known utility. There is no disclosure in the specification of any . . . antagonists of pharmacological significance that have been shown to specifically bind and modulate calcium flux through the T-type calcium channel of SEQ ID NO:23. . . . There is no disclosure that . . . an antagonist will be beneficial." Examiner's Answer, page 4.

The examiner notes that "[t]he specification discloses conditions associated with calcium channels . . . [but] the question is what specific disease state is associated with dysfunction of the ion channel of SEQ ID NO:23. . . . Determining which compounds interact with T-type ion channel of SEQ ID NO:23 do not provide a utility for the ion

channel or the method of its use, it is just a method to discover the functionality of the ion channel." Examiner's Answer, pages 4-5.[1] The examiner cites Ertel[2] as evidence that "[a] compound that acts as an . . . antagonist on the α1 T-type channel protein used in the claimed method may not have the same effect on other α1 T-type channel proteins" and that "compounds may have different effects depending on their concentration." Id., page 9.

Appellants argue that the evidence of record shows that "T-type calcium ion channel modulators do have clinical function." Appeal Brief, page 7. Appellants cite references disclosing that mibefradil is a selective antagonist of T-type calcium channels and has been used to treat hypertension and congestive heart failure, among other things. Appeal Brief, pages 7-8. Appellants also cite the declaration of Terrance Snutch (submitted March 26, 2004). Dr. Snutch declares that T-type calcium channels were known to be associated with various cardiac and neurological conditions. Declaration, pages 1-2; Appeal Brief, pages 8-9.

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence.").

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[1] The examiner also takes issue with the use of sequence homology to identify the protein encoded by SEQ ID NO:23 as a calcium channel. See the Examiner's Answer, pages 12-15. However, the examiner later states: "In [the] instant case Examiner is not arguing that alpha 1 subunit of the SEQ ID NO:23 is not a T-Type calcium channel." Id., page 19. As we understand it, the examiner does not dispute that SEQ ID NO:23 encodes a T-type calcium channel subunit.

[2] Ertel et al., "Low-voltage-activated T-type Ca^{2+} channels," TiPS, Vol. 18, pp. 37-42 (1997).

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement as it applies to DNA. See In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court held that § 101 requires a utility that is both substantial and specific. Id. at 1371, 76 USPQ2d at 1229. Disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." Id., at 76 USPQ2d at 1230.

A specific utility is "a use which is not so vague as to be meaningless." Id. In other words, "in addition to providing a 'substantial' utility, an asserted use must show that th[e] claimed invention can be used to provide a well-defined and particular benefit to the public." Id.

In this case, we conclude that a preponderance of the evidence of record supports Appellants' position rather than the examiner's. There is no dispute that SEQ ID NO:23 is a subunit of a T-type calcium channel. The specification provides working examples that are said to show that the protein of SEQ ID NO:23 has the properties of a α_1 subunit of a T-type calcium channel (pages 24-26) and the examiner has not disputed the accuracy of that conclusion. The examiner, in fact, has stated that the function of SEQ ID NO:23 is not in dispute ("Examiner is not arguing that alpha 1 subunit of the SEQ ID NO:23 is not a T-Type calcium channel," Examiner's Answer, page 19).

The utility asserted for the instantly claimed method is directly related to the function of the protein of SEQ ID NO:23. That is, the compounds identified in the

claimed assay are asserted to be useful because they have the property of antagonizing the function of the T-type calcium channel that includes SEQ ID NO:23, the α_1 subunit.

The evidence of record shows that at least some antagonists of T-type calcium channels are clinically useful. For example, Ertel states that "promising new drugs are being developed, which block T channels. Many are CNS drugs that target epilepsy, where T channels are believed to trigger repetitive firing." Page 37, left-hand column. See also page 41, middle column ("anti-convulsants are probably the most prolific therapeutic field for T-channel blockers"). Ertel also states that mibefradil is a "antihypertensive, antianginal Ca^{2+} channel antagonist . . . which has the unique property of blocking preferentially T channels." Id.

Appellants have submitted abstracts from several research papers that describe use of mibefradil in treating hypertension, congestive heart failure, and ischemic left ventricular dysfunction; as a vasodilator; and for preventing neointima formation. See Exhibits A-F attached to the Appeal Brief (references originally filed March 26, 2004). Appellants have also submitted the abstract from a paper that describes "the effects of zonisamide, a new antiepileptic drug, on voltage-dependent T-type calcium current . . . in cultured neuroblastoma cells. . . . The blockage of T-type calcium channels by zonisamide could . . . inhibit[ ] the spread of seizure activity." Exhibit G attached to the Appeal Brief.

The evidence of record therefore shows that antagonists of T-type calcium channels are known in the art for treating specific conditions. Based on the known utility of other T-type calcium channel antagonists, those skilled in the art would reasonably

expect that at least some of the compounds identified using the instantly claimed method would be useful as therapeutic agents.

The Snutch declaration supports this expectation. Dr. Snutch has stated that

> compounds which are found to inhibit or stimulate the activity of nervous T-type channels will also inhibit or stimulate the activity of T-type channels found in other tissues. Thus any arbitrarily chosen T-type channel could be expressed in a cell line for use in screening assays to identify agonists or antagonists and the agonists or antagonists would be useful in treating the conditions associated with any T-type channel.

¶ 3.

The examiner disputes this assertion, arguing that an antagonist of the protein of SEQ ID NO:23 may not have the same effect on other T-type calcium channels. Examiner's Answer, pages 15-16. In support of this position, the examiner cites Ertel's disclosure that "Ni^{2+} blocks T channels but it is difficult to predict the actual potency of Ni^{2+} block and it is risky to rely on it to classify an expressed channel as T-type." Id., page 16.

We do not agree with the examiner's interpretation of Ertel. Ertel summarizes the presentations at a workshop devoted to T-type calcium channels. Ertel discloses that "[t]he pharmacology of T channels was . . . heavily discussed as a means to recognize them." Page 37, middle column. In that context, Ertel reports that researcher Gerald Zamponi "found that Ni^{2+} block [of T-type channels] is . . . a combination of four actions: a reduction in the peak current, a slowing of activation, a slowing of inactivation, and a shift of the voltage dependence of the channels towards more positive values." Page 37, right-hand column. Zamponi found that "[a]s each of these actions appears to depend differently on the molecular composition of the expressed

channels and on the experimental conditions, it is difficult to predict the actual potency of Ni^{2+} block and it is risky to rely on it to classify an expressed channel as T-type." Id.

The passage quoted by the examiner does not address the potential therapeutic use of T-type calcium channel antagonists. Rather, the part of the reference cited by the examiner focuses on identifying calcium channels as T-type channels based on their interaction with different calcium channel antagonists. Therefore, we do not agree with the examiner that Ertel's discussion of the effect of Ni^{2+} in blocking T-type channels would have led those skilled in the art to doubt the potential therapeutic utility of T-type calcium channel antagonists.

The instant claims are directed to a screening assay, not to specific chemical compounds. The claimed assay can be useful even if, as would undoubtedly be the case, many of the compounds identified as T-type channel antagonists turn out not to be therapeutically useful. The utility of the claimed method is in directing drug screening research toward compounds that are more likely to have an activity that will make them therapeutically useful.

The instant claims are different from, for example, the expressed sequence tags (ESTs) at issue in In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The ESTs claimed by Fisher were derived from genes of unknown function. See id. at 1373, 76 USPQ2d at 1231. Fisher argued that an EST is a research tool, like a microscope, and therefore useful. Id. The court disagreed:

> [A] microscope has the specific benefit of optically magnifying an object to immediately reveal its structure. One of the claimed ESTs, by contrast, can only be used to detect the presence of genetic material having the same structure as the EST itself. It is unable to provide any information about the overall structure let alone the function of the underlying gene.

Id. The court concluded that

> the claimed ESTs act as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. . . . Accordingly, the claimed ESTs are . . . mere 'object[s] of use-testing,' to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end.

Id.

Thus, the ESTs claimed in Fisher were held to lack utility because they were not useful for conducting research generally, but only for conducting research on the ESTs themselves and the genes from which they were derived. Here, by contrast, the evidence of record shows that the claimed assay method is useful for identifying compounds that are likely to block T-type calcium channels generally, rather than only the T-type calcium channel subunit of SEQ ID NO:23. The evidence of record also shows that known T-type calcium channel antagonists are useful for treating a variety of conditions. The evidence therefore provides a reasonable basis for expecting that the claimed method would be useful for identifying other compounds useful for treating the same conditions.

In summary, the evidence of record does not support the examiner's position that the claimed assay lacks patentable utility. The rejections under 35 U.S.C. §§ 101 and 112, first paragraph, are reversed.

Other Issue

The present application was filed July 2, 1999 and claims the benefit under 35 U.S.C. § 120 of application 09/030,482, filed February 25, 1998. Specification, page 1.

The claims in the present application require the use of "[an] α_1 subunit . . . functional as a T-type calcium channel and . . . encoded by a nucleotide sequence which hybridizes under [specified] conditions of stringency . . . to a nucleic acid comprising SEQ ID NO:23." SEQ ID NO:23 is a full-length cDNA (7540 nucleotides long) encoding the rat α_{1G} subunit of a T-type calcium channel. Page 16, lines 1-11.

The parent '482 application states that it "provides partial sequences" for human and rat calcium channel α_{1I} subunits and a human calcium channel α_{1H} subunit. Page 8, lines 2-4. The '482 application does not appear to disclose nucleotide sequences encoding an α_{1G} subunit, and does not disclose any sequence that is 7540 nucleotides in length.

Therefore, the claims on appeal do not appear to be supported by the earlier application in the manner required by 35 U.S.C. § 112, first paragraph. Lacking such support, the present claims would not be entitled to the benefit of priority under 35 U.S.C. § 120 based on the earlier-filed application; the effective filing date of the claims appears to be July 2, 1999.

Perez-Reyes[3] discloses "the amino acid sequences of full-length T-type channels, and the sequences of suitable coding nucleic acids . . . at SEQ ID NOs:1-8 (α1G sequences)." Page 6, lines 5-7. Perez-Reyes indicates that SEQ ID NO:5 is derived from rat ("Rattus sp."). See page 37. Amino acids 33 to 2254 of the sequence encoded by Perez-Reyes' SEQ ID NO:5 appear to be virtually identical to amino acids 65 to 2287 of the sequence encoded by the present application's SEQ ID NO:23.

[3] Perez-Reyes et al., WO 99/29847, published June 17, 1999, submitted with the Information Disclosure Statement filed March 15, 2001

Perez-Reyes discloses a

> method of identifying a drug which affects T-type calcium channels. The method involves first expressing a T-type calcium channel in a cell to produce an active channel. . . . The cell expressing the channel is then exposed to a solution containing a putative drug for interfering with the channel. Thereafter, the presence or absence of calcium flux in response to a change in membrane potential is assayed.

Page 11, lines 7-12.

Perez-Reyes also includes a working example showing that "mibefradil almost completely abolished T-type current in cells expressing α1G." Page 18. The example is said to "demonstrate[ ] that a cloned T-type calcium channel can be used for identifying a drug which affects T-type calcium channels." Id. Thus, Perez-Reyes reasonably appears to disclose a method of identifying drugs that affect T-type calcium channels using cells expressing a rat α1G calcium channel subunit.

However, Perez-Reyes does not reasonably appear to disclose the specific methods defined by claims 28 and 31, the only independent claims remaining in the present application. Claim 28 requires contacting a recombinant cell expressing an α1G subunit "with a known agonist of [a] T-type calcium channel," while claim 31 requires determining binding of a test compound to a cell expressing an α1G subunit "by observing competitive binding with a known agonist or antagonist of [a T-type calcium] channel."

Perez-Reyes does not disclose either of these limitations and therefore does not appear to anticipate the presently pending claims. On return of this application, however, we recommend that the examiner consider the differences between the method disclosed by Perez-Reyes and the methods defined by the pending claims. If

the examiner believes that the differences are such that the claimed methods would have been obvious in view of the prior art method, a rejection based on 35 U.S.C. § 103 should be entered. If a new rejection is made, of course, Appellants must be given an appropriate opportunity to respond.

REVERSED

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